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**SRY-box-containing gene 2 regulation of nuclear receptor tailless (Tlx) transcription in adult neural stem cells.**

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**Public Summary:**

Adult neurogenesis is maintained by self-renewable neural stem cells (NSCs). Their activity is regulated by multiple signaling pathways and key transcription factors. However, it has been unclear whether these factors interplay with each other at the molecular level. Here we show that SRY-box-containing gene 2 (Sox2) and nuclear receptor tailless (TLX) form a molecular network in adult NSCs. We observed that both Sox2 and TLX proteins bind to the upstream region of Tlx gene. Sox2 positively regulates Tlx expression, whereas the binding of TLX to its own promoter suppresses its transcriptional activity in luciferase reporter assays. Such TLX-mediated suppression can be antagonized by overexpressing wild-type Sox2 but not a mutant lacking the transcriptional activation domain. Furthermore, through regions involved in DNA-binding activity, Sox2 and TLX physically interact to form a complex on DNAs that contain a consensus binding site for TLX. Finally, depletion of Sox2 revealed the potential negative feedback loop of TLX expression that is antagonized by Sox2 in adult NSCs. These data suggest that Sox2 plays an important role in Tlx transcription in cultured adult NSCs.

**Scientific Abstract:**

Adult neurogenesis is maintained by self-renewable neural stem cells (NSCs). Their activity is regulated by multiple signaling pathways and key transcription factors. However, it has been unclear whether these factors interplay with each other at the molecular level. Here we show that SRY-box-containing gene 2 (Sox2) and nuclear receptor tailless (TLX) form a molecular network in adult NSCs. We observed that both Sox2 and TLX proteins bind to the upstream region of Tlx gene. Sox2 positively regulates Tlx expression, whereas the binding of TLX to its own promoter suppresses its transcriptional activity in luciferase reporter assays. Such TLX-mediated suppression can be antagonized by overexpressing wild-type Sox2 but not a mutant lacking the transcriptional activation domain. Furthermore, through regions involved in DNA-binding activity, Sox2 and TLX physically interact to form a complex on DNAs that contain a consensus binding site for TLX. Finally, depletion of Sox2 revealed the potential negative feedback loop of TLX expression that is antagonized by Sox2 in adult NSCs. These data suggest that Sox2 plays an important role in Tlx transcription in cultured adult NSCs.

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